Ovarian Cancer: A Bright Future

It is easy to understand why epithelial ovarian cancer (EOC) is such a dreaded disease. It remains one of the most lethal of cancers to affect women. Although the second most common gynecologic cancer, it has the highest mortality rate. While it ranks 9th in incidence among all cancers in women, it is the 4th leading cause of cancer death.1 Broad, effective screening is not available, and the majority of patients with EOC are diagnosed at an advanced stage. And while the majority of these patients will have a complete clinical response to initial surgery and chemotherapy, over 85% will relapse and ultimately develop resistant disease.

Despite these grim statistics, it should be recognized that real progress has been made in the treatment and understanding of EOC. Consider the improvement in median overall survival time for women with advanced EOC during the last three decades. Clinical trials have led to advances in surgery and also to improvements in chemotherapy drugs and delivery.2,3 Such advances have resulted in increased median overall survival from 17 months to over 65 months. Increasingly, we are witnessing advances in our understanding of the cellular and molecular biology that underlies EOC development, progression, and response to therapy. Such knowledge has enabled us to enter the era of biologically targeted therapy — with many of these new drugs demonstrating activity in EOC.

In our first article in this issue, Drs Chon and Lancaster describe how DNA microarray technology has enhanced insight into EOC via genomic expression profiling. This tool has been useful in clustering tumor types according to molecular classifications, providing an understanding that goes well beyond histology alone. The technology has also yielded information that has implications in screening for the disease. A notable example is the cited work by Berchuck et al,4 suggesting that advanced cancers with a good prognosis are similar at a genomic level to cancers diagnosed at an early stage. This seems to support the idea that early diagnosis is more a function of biology than timing, as some researchers and clinicians in this field have suspected. DNA microarray has been effective as a prognosticator of recurrence and survival. The authors go on to describe the effort to develop predictive profiles that may ultimately guide our treatment of patients. Applications such as the Oncotype DX and MammoPrint for breast cancer are obvious proof of principal examples that such an effort in EOC will surely be fruitful.

Despite the enormous effort of talented investigators, an effective screen for EOC that improves prognosis remains elusive. Dr Cragun examines what has been learned in these endeavors. The development of symptom indices, ultrasound, physical examination, and tumor markers has not overcome the stringent requirements of specificity, sensitivity, and positive and negative predictive values for a disease of such low prevalence and variable biology. There is clear frustration associated with this, and many professional organizations and guidelines still advocate for screening in some populations despite an unclear benefit of doing so. I, like others, remain hopeful that we will make significant progress in screening as technology advances and new assays become available.

Surgery has had a pivotal role in the management of patients with EOC. In the next article, Drs Ramirez, Chon, and Apte describe the association between improved outcomes and better cytoreductive surgery. While no prospective randomized trial has compared surgery plus chemotherapy to chemotherapy alone, it is likely that the weight of data supporting a benefit to surgery would make such a study difficult to carry out. On the other hand, new data fuel the controversy surrounding the ideal timing of surgery relative to chemotherapy; with recent evidence demonstrating the noninferiority of neoadjuvant chemotherapy with interval rather than primary cytoreductive surgery in patients with preoperative findings suggestive of very advanced disease.5 The authors also examine surgery for second looks, secondary cytoreduction, bowel obstruction, and minimally invasive surgery.

The antiangiogenetics comprise one of the more exciting new classes of drugs being evaluated in patients with EOC (and cancers in general). Drs Teoh and Secord review the rapidly accumulating information on these agents. Preclinical data demonstrate that alterations in the angiogenic pathway are predictive of outcome. And while readers will likely be familiar with some of the clinical data regarding the anti-VEGF antibody bevacizumab (Avastin) and its activity in primary and recurrent EOCs, other promising but lesser-recognized agents are emerging. These include drugs such as fusion proteins, tyrosine kinase inhibitors, and peptibodies that target various components of the angiogenic pathway.

Drs Gardner and Jewell summarize the current state of clinical trials for EOC, placing today’s trials in the context of earlier work. They cover a broad range of the important studies and highlight some sentinel findings that led to shifts in treatment paradigms for EOC. They also discuss many recent and ongoing trials that examine the timing of surgery, the use of novel agents,
Shammo and his coauthors recognize this lacuna, so he and his group reviewed the areas where educational interventions might minimize these deficiencies. Seven areas were identified and placed in priority pertinent to the different groups of clinicians who are involved in caring for patients with MDS. Attention to these recommendations should result in further improvement in outcomes for this disease.

Robert M. Wenham, MD, FACOG, FACS
Gynecologic Oncology and Experimental Therapeutics Programs
H. Lee Moffitt Cancer Center & Research Institute
Tampa, Florida
E-mail: Robert.Wenham@moffitt.org

References